

Low Intensity Extracorporeal Shock Wave Therapy for Female Stress Urinary Incontinence Using a Vaginal Probe: A Single-Blind, Randomized-Controlled Trial

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Background – 1

Low intensity extracorporeal low energy shock wave therapy (LiESWT)

- Clinical LiESWT (2000 to 3000 pulses in 0.20–0.25 mJ/mm²) induces tissue regeneration by:
 - Enhancement of wound healing
 - Promotion of angiogenesis
 - Reduced level of oxidative stress
 - Induction of vascular endothelial growth factor (VEGF) release
 - Proliferation and differentiation of stem cells
- A vast body of evidence has proved LiESWT is effective in treating:
 - Tendon-bone junction diseases,
 - Ischemic cardiovascular disorders
 - Skin wound healing
 - Chronic prostatitis/chronic pelvic pain syndrome (CP/ CPPS)
 - Chronic injuries of soft tissues and
 - Erectile dysfunction

Background – 2

Effect of LiESWT in female LUTS: Pre-clinical studies

Stress urinary incontinence

Sprague–Dawley/Zucker Lean rats
Vaginal balloon dilation-induced SUI

Urodynamic studies:

increased LPP

Immunohistochemical studies:

Promotion of urethral myogenesis
Increased urethral angiogenesis

Wang et al, Neurourol Urodyn. 2018; Wu et al, Transl Androl Urol. 2018; Zhang et al, Urology. 2020

Overactive bladder

Sprague–Dawley rats
Ovariectomy-induced OAB

Urodynamic studies:

significantly improved bladder storage function

Immunohistochemical studies:

improved bladder damages-
thicker layer of urothelium
Reduction of interstitial fibrosis

Lin et al, Int J Mol Sci. 2021,

Detrusor underactivity

Sprague–Dawley rats
Streptozotocin-induced DM

Urodynamic studies:

enhanced bladder muscle contractile activity

Immunohistochemical studies:

higher smooth muscle actin expression
recovery of neuronal integrity and innervation

Wang et al, BJU Int. 2018

Background – 3

Effect of LiESWT in female SUI: Clinical studies

Therapeutic effects of Low intensity extracorporeal low energy shock wave therapy (LiESWT) on stress urinary incontinence

Cheng-Yu Long^{1,2,3,4,11}, Kun-Ling Lin^{1,4,11}, Yung-Chin Lee^{5,6,7}, Shu-Mien Chuang^{5,8}, Jian-He Lu^{5,7}, Bin-Nan Wu⁹, Kuang-Shun Chueh^{5,10}, Chin-Ru Ker¹, Mei-Chen Shen⁵ & Yung-Shun Juan^{3,5,7,10*}



- **Single arm, open-label, prospective**
- 50 subjects, SUI with leakage urine ≥ 2 g on physical activity.
- LiESWT once a week for 8 wks, to the labia minora, 1 month follow-up
- DUOLITH SD1-TOP focused shock wave system (STORZ MEDICAL AG).

Results:

- Significant decrease in leaked urine amount on pad test: 3.60 ± 1.01 ($p < 0.01$) and 0.89 ± 0.31 ($p < 0.01$)
- Improved functional bladder capacity
- Improved scores on questionnaires: OAB-SS, ICIQ, UDI-6, IIQ-7

- **Multicenter, single-blind, sham-controlled RCT**
- 60 subjects, SUI or SUI-predominant MUI > 3 months
- LiESWT once a week for 8 wks, to the labia minora, 6 months follow-up
- DUOLITH SD1-TOP focused shock wave system (STORZ MEDICAL AG).

Results:

- Pad test: No change in sham vs significant in LiESWT. ($p = 0.004$)
- Improved scores in ICIQ-SF ($p = 0.034$), UDI-6 ($p = 0.040$), and IIQ-7 ($p = 0.048$), no change in OAB-SS
- 84.5% of patients had >50% improvement at 6 months in study group

Objective

The objective of the study was to assess safety and efficacy of LiESWT using a novel *trans-vaginal probe* for SUI and sexual function (SF).



Methods – 1

Single-blind, randomized-controlled trial

IRB approval, informed consent

Women with mild to moderate SUI were randomly assigned to

- LiESWT with 0.1 mJ/mm² intensity, 1600 pulses, twice weekly for 4 weeks
- LiESWT was delivered for a total of 16 minutes towards 4 points below the urethra, by rotating the probe every 4 minutes by approximately 20 degrees
- Sham treatment, without energy transmission.
- Treatment:sham ratio- 2:1

Both were administered by a vaginal probe (MoreNova^{FEM}, Hikkonu Medical Systems Ltd, Ramat Hasharon, Israel), designed to deliver the pulses towards the peri-urethral tissue



Methods– 2

Inclusion criteria:

- Age 20-75
- SUI diagnosis according to history and positive cough-stress test
- PVR < 50 cc

Exclusion criteria:

- Pregnancy or breastfeeding
- Severe SUI (1-hour pad test >50 grams)
- POP beyond the hymen
- MUI with a predominant urgency component (UDI-6 questions 1 or 2 scoring 3 or 4)
- History of vaginal fistula; perineal tear grade 4; CPP; GPPPD; genital HSV; active STI; IBD; psychiatric conditions preventing informed consent; therapies affecting bladder function

Methods – 3

Efficacy at 1 month and 6 months post-treatment was evaluated using:

Patient Global Impression of Improvement (PGI-I)

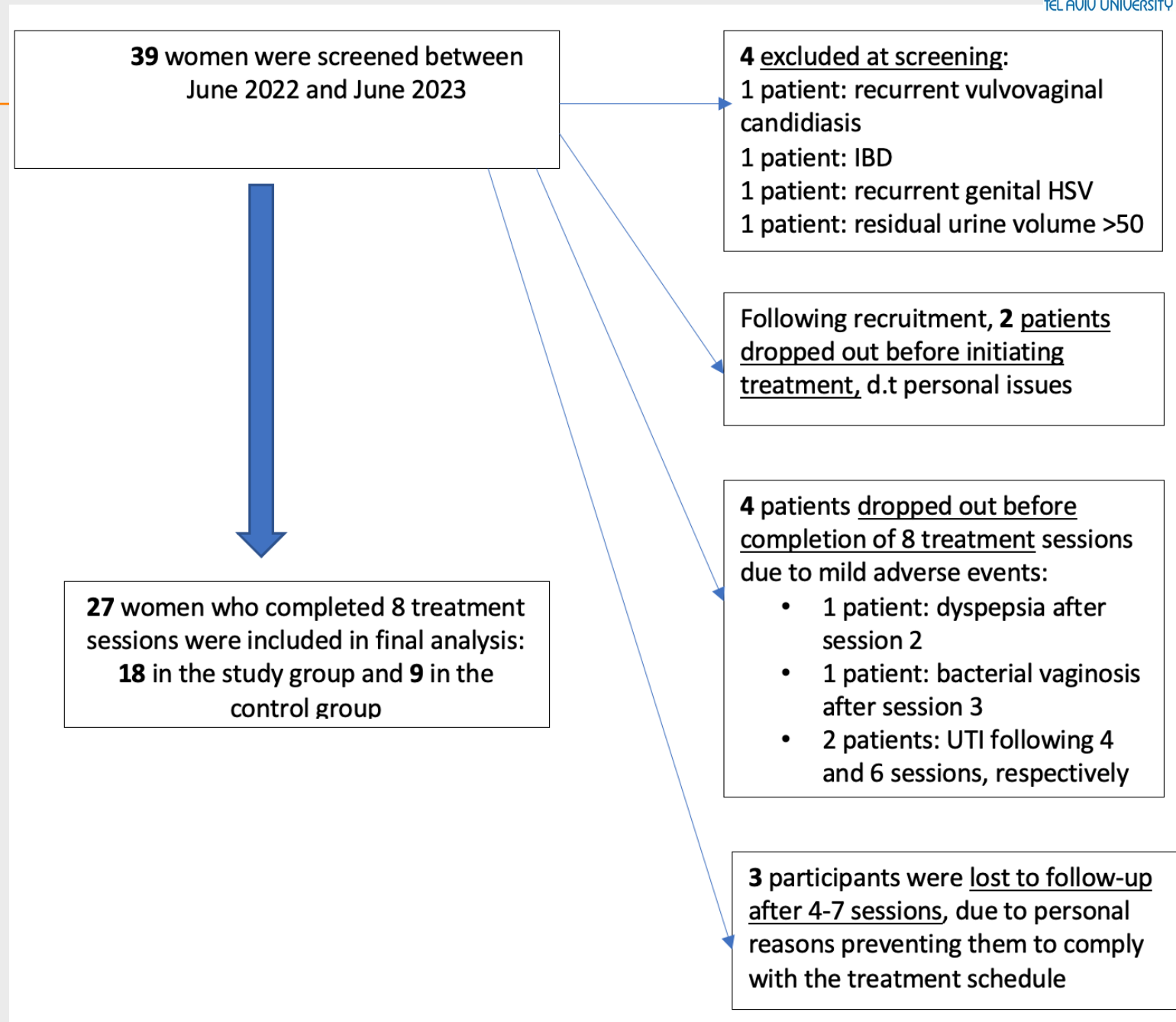
Changes from baseline in scores of:

- International Consultation on Incontinence, Short Form (ICI-Q-SF)
- Urinary Distress Inventory (UDI-6)
- Incontinence Impact Questionnaire (IIQ-7)
- Cough-stress test
- 1-hour pad test.

SF was evaluated by the Pelvic Organ Prolapse/Urinary Incontinence Sexual Questionnaire, IUGA-Revised (PISQ-IR).

Results – 1

Study flowchart



Results – 2

Table 1- Background data

Variables	Sham (N=9)	Treatment (N=18)	P Value
Age (Y)	46.4±9.8	50.1±8.6	0.3404
BMI	27.3±4.4	25.1±3.7	0.1729
Diabetes	0	2 (11.1)	0.1729
Hypertension	2 (22.2)	2 (11.1)	0.5815
Smoking	0	1 (5.6)	1.0000
Parity	3.0 (2.0–3.0)	3.0 (2.0–3.0)	0.8066
Post-menopausal	4 (44.4)	7 (38.9)	1.0000
HRT	0	1 (5.6)	1.0000
Vaginal Estrogen	0	2 (11.1)	0.5385

Pain visual analogue scale (VAS) at treatment n. 8 was 0.6 ± 1.0 and 0.1 ± 0.3 , $p = 0.2146$.

Results – 3

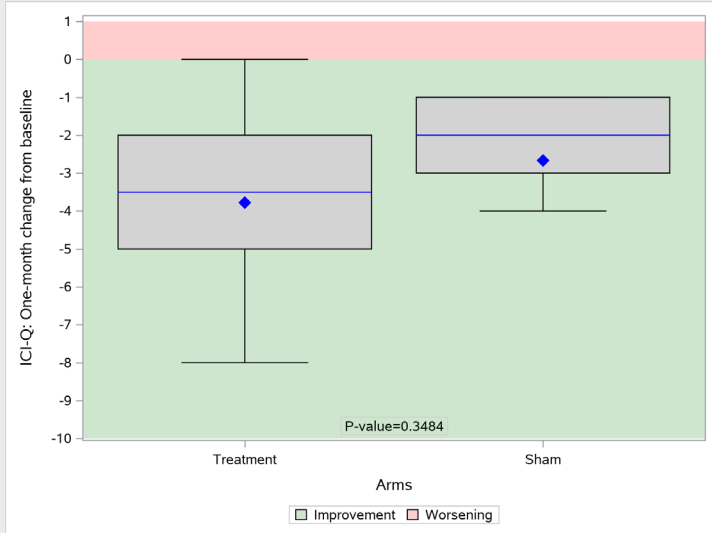
- Both at the 1-month and 6-month follow-up, significantly greater improvement in IIQ-7 scores was observed in the treatment group compared to sham.
- At the 6 month- follow-up, we observed a greater improvement in the one-hour pad test in the treatment group, with borderline statistical significance -1.9±3.8 grams vs. 0.5±3.5 grams, respectively (p=0.055)
- Changes in urinary and sexual function were otherwise similar between groups
- Possible procedure-related adverse events were mild, and patients fully recovered: spotting (2 women, study group), UTI (1- study group, 1- sham), bacterial vaginosis (1- study group)**

Variables	1-month follow-up			6-months follow-up		
	Sham (N=9)	Treatment (N=18)	P Value	Sham (N=9)	Treatment (N=18)	P Value
cough-stress test status			>0.99			0.657
- No change	6 (66.7)	10 (66.7)		7 (77.8)	9 (64.3)	
- Negative at baseline and positive at follow-up	0 (0.00)	0 (0.00)		0 (0.00)	0 (0.00)	
- Positive at baseline and negative at follow-up	3 (33.3)	5 (33.3)		2 (22.2)	5 (35.7)	
change in 1-hour pad test			0.8505			0.0552
Nmiss (%)	1 (11.1)	2 (11.1)		1 (11.1)	4 (22.2)	
Mean±SD	-1.4±4.4	-0.3±3.4		0.5±3.5	-1.9±3.8	
Min-Max	-11.0-4.0	-4.0-11.0		-2.0-9.0	-12.0-6.0	
Median (IQR)	-0.5 (-2.0-0.5)	-1.0 (-1.5-0.0)		-0.5 (-1.0-0.0)	-1.0 (-3.0-1.0)	
change in ICI-Q			0.3484			0.6448
Mean±SD	-2.7±1.9	-3.8±3.0		-3.1±3.0	-3.6±3.4	
Min-Max	-7.0-1.0	-11.0-0.0		-9.0-1.0	-11.0-2.0	
Median (IQR)	-2.0 (-3.0-1.0)	-3.5 (-5.0-2.0)		-3.0 (-4.0-1.0)	-4.0 (-6.0-1.0)	
change in UDI-6			0.9794			0.4997
Mean±SD	-11.9±15.6	-11.2±14.3		-8.7±15.3	-7.1±14.5	
Min-Max	-46.0-5.0	-46.0-8.0		-33.0-25.0	-33.0-25.0	
Median (IQR)	-8.0 (-20.0-0.0)	-10.5 (-17.0-0.0)		-10.0 (-13.0-5.0)	-8.0 (-16.0-2.0)	
change in IIQ-7			0.0239			0.0459
Mean±SD	-1.0±7.3	-15.9±25.8		-3.1±9.6	-15.6±23.9	
Min-Max	-10.2-15.0	-100.0-23.9		-19.0-14.6	-95.3-9.6	
Median (IQR)	0.0 (-4.7-0.0)	-12.0 (-19.1--0.1)		0.0 (-4.7-0.0)	-9.5 (-19.1-4.8)	
change in PISQ-IR			0.854			0.0644
Nmiss (%)	1 (11.1)	2 (11.1)		1 (11.1)	5 (27.8)	
Mean±SD	0.1±0.3	0.1±0.3		0.2±0.3	0.0±0.2	
Min-Max	-0.4-0.5	-0.7-0.6		-0.2-0.6	-0.3-0.4	
Median (IQR)	0.1 (-0.2-0.4)	0.1 (-0.0-0.2)		0.3 (0.1-0.4)	0.0 (0.0-0.1)	
PGI-I at follow-up			>0.99			>0.99
Improvement (1-2)	1 (14.3)	4 (25.0)		3 (33.3)	5 (29.4)	
No change (3-5)	6 (85.7)	12 (75.0)		6 (66.7)	12 (70.6)	
Worsening (6-7)	0 (0.0)	0 (0.0)		0 (0.0)	0 (0.0)	

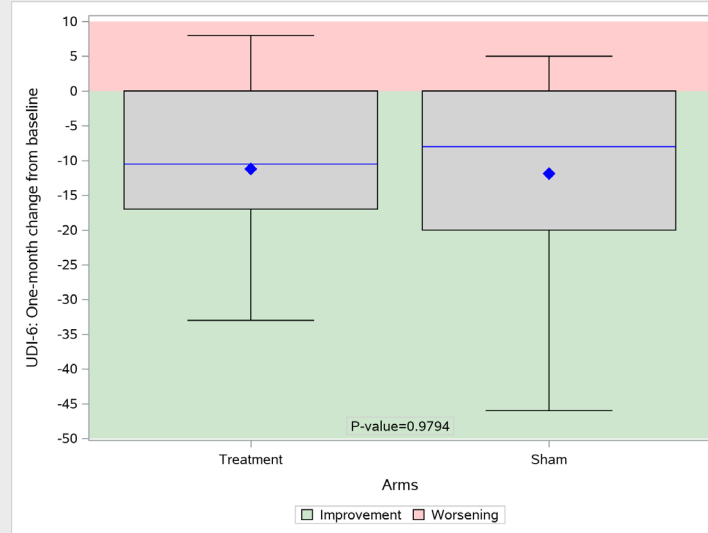
Results – 4

1-month follow-up

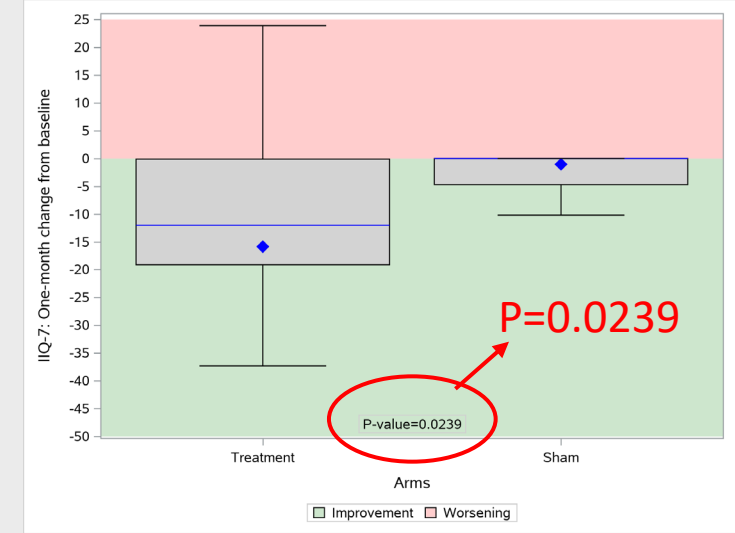
ICI-Q



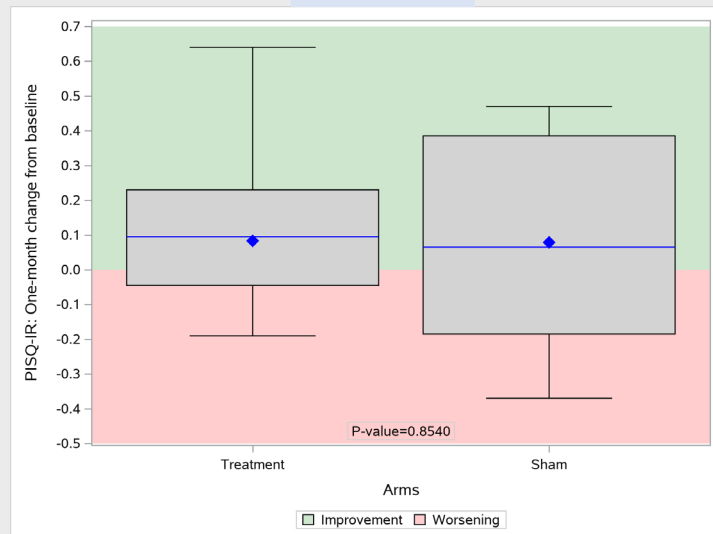
UDI-6



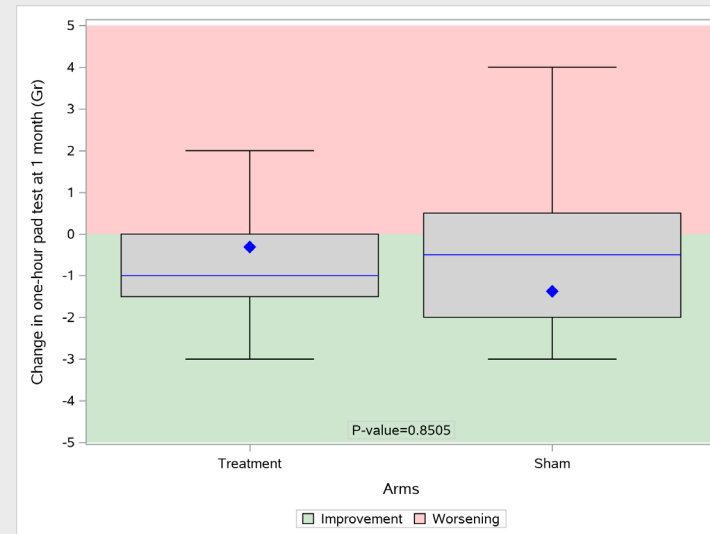
IIQ-7



PISQ-IR



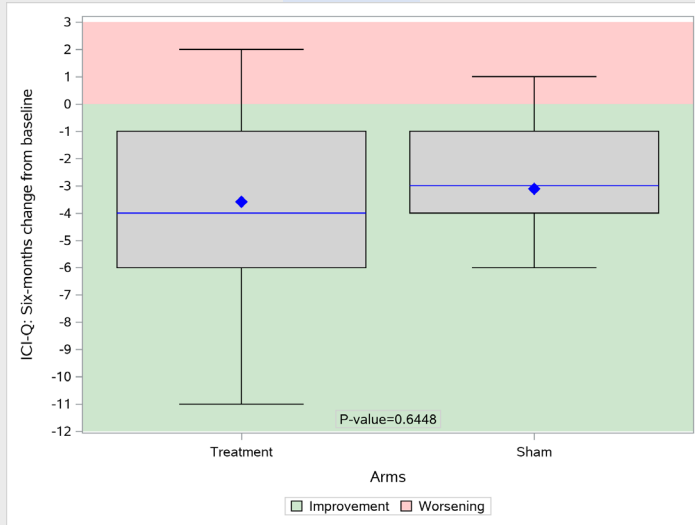
One-hour pad test



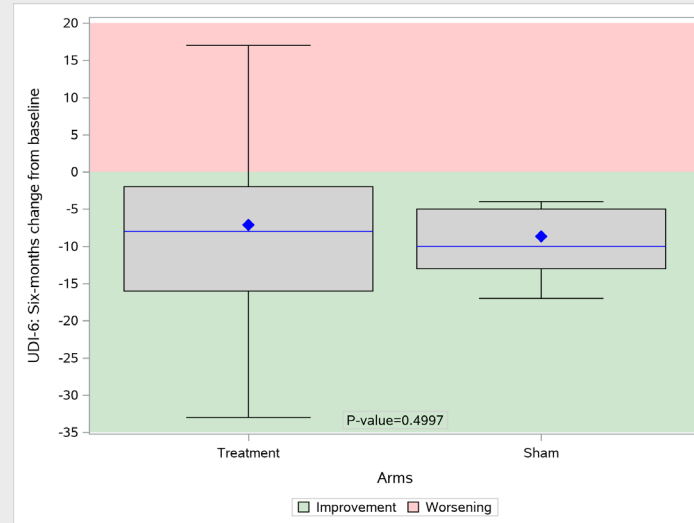
Results – 5

6-month follow-up

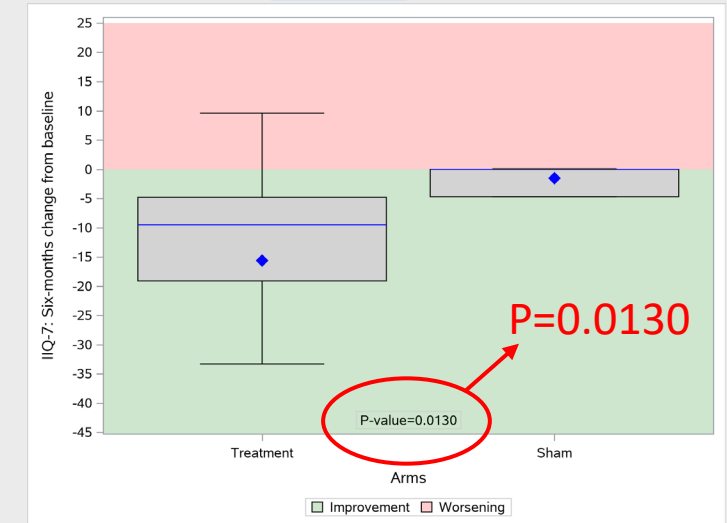
ICI-Q



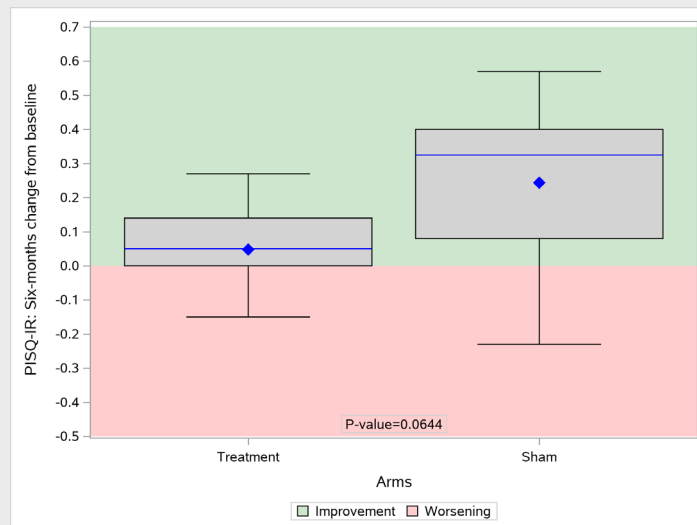
UDI-6



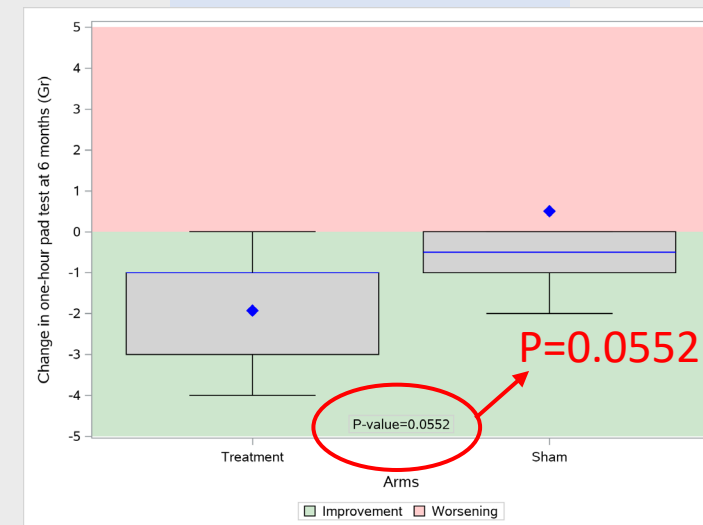
IIQ-7



PISQ-IR



One-hour pad test



Conclusions



We have shown that LiESWT is feasible and well tolerated by women, causing no discomfort or pain



The treatment has proved safe on 6-months follow-up, with few and mild procedure-related adverse events



At the 6-months follow-up, we observed a greater improvement in the amount of urine leakage in the treatment arm, assessed by the 1-hour pad test



We also observed a greater improvement in the impact of SUI on quality of life in the treatment arm 1 month and 6 months following treatment completion, as reflected by a significant decrease in IIQ-7 scores

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Thank you for your attention! Questions?

